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The Determination of Narcotine and Meconic Acid in Opium. Third Method.

(A Report from the Government Laboratory, London, England)
By J. R. Nicholls and E. G. Kellett

In continuation of the international programme of scientific research undertaken pursuant to resolution 246 F (IX), adopted by the Economic and Social Council on 6 July 1949, the Secretary-General is now publishing three articles, Nos. 5, 6, and 7 in this series, on the determination of narcotine and meconic acid in opium. These three articles present three different methods successively worked out at the Government Laboratory, London, England. The Secretary-General has considered that the first two methods include features which may be suggestive and helpful to the chemists working on opium, and that they are so different from the third method as to warrant separate publication. However, the third method, which is the present paper, to a great extent supersedes the first two. It is believed to be the easiest of the three to carry out, and also to give the most accurate results.

The Determination of Narcotine and Meconic Acid in Opium, Third Method.

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Summary

1. Narcotine present in opium as free base or as a readily dissociated salt is quickly and cleanly extracted by cold acetone.

2. All the narcotine not extracted as under 1. is easily extracted by subsequent treatment with water only.

3. From a neutral or slightly alkaline aqueous solution of a narcotine salt, narcotine is precipitated quantitatively on saturation with sodium acetate. In the presence of 25 per cent of ethanol or methanol, such precipitation, though not complete, is nearly so; and, in this case, even in the presence of other opium extractives, the narcotine separates in crystalline and substantially pure state.

4. Extraction of meconic acid from opium by direct treatment with water is slow and incomplete. With dilute acetic or mineral acids (about N/5) extraction is complete but still slow. After exhausting the opium with acetone, however, the meconic acid can be extracted in warm water without undue difficulty, and in a purer state than by acid extraction.

5. From slightly alkaline solutions, meconic acid is precipitated by barium ion as barium meconate.

6. From solutions alkaline to phenolphthalein, trisodium meconate can be almost completely precipitated by salting out with sodium ion. Trisodium meconate titrates as a mono-acid base to bromphenol blue.

Discussion

7. Most of the narcotine in opium is easily extracted by acetone, unaccompanied by any notable amount of other extractives except for a neutral gummy material insoluble in acids and hence easily separated from the narcotine. With some opiums it has been found that, even after exhaustive percolation with acetone, a small amount of narcotine remains in the opium, from which it is then easily extracted with water. It seems possible that this may correspond to the presence of narcotine partly as easily-dissociated salt such as meconate, and partly as a

/salt of

salt of a stronger acid such as sulphuric. This point is under further investigation.

8. For purposes of determining the total narcotine, that present in the aqueous extract is precipitated by addition of sodium acetate; narcotine is washed out of this precipitate with acetone and added to the main portion already obtained by direct acetone extraction.

9. A rapid though not perfectly complete separation of the narcotine from opium may be effected by extracting it with dilute acid, adding to the extract one third of its volume of ethanol or methanol, and stirring in sodium bicarbonate, until a little remains undissolved. Narcotine separates in crystals and is determined by filtering these off, washing with dilute caustic alkali and with water, then washing through with acetone and evaporating with acetone solution.

10. When narcotine is precipitated with sodium acetate from the aqueous extract of opium, as described above, a little calcium meconate may also be precipitated and remains undissolved on subsequent washing with acetone. The main bulk of the meconate is precipitated by barium chloride. From the calcium and barium meconate combined, meconic acid is liberated by the action of a small volume of dilute sulphuric acid; and from the resulting solution trisodium meconate is precipitated and titrated as indicated in the Summary, paragraph 6. The volume of solution can be kept so small as to render the solubility correction insignificant.

11. Representative results obtained by the above procedure are:

	% Narcotine	% Meconic acid
India - League of Nations 1935, I	4.5	2.0
" " " " II	5.7	3.0
Iran " " " " III	7.8	5.0
Another sample	7.4	5.4
Turkey - League of Nations 1935 IV	4.4	4.3
Another sample	2.95	3.0
Yugoslavia - League of Nations 1935 V	3.5	5.5
Another sample	2.4	3.4

12. It appears possible that the narcotine/meconic acid ratio may be a characteristic of the type of opium and it is hoped to give further attention to this point when more figures for "total" and "acetone-soluble" narcotine have been obtained.

/Experimental

Experimental:

I. Extraction of narcotine and meconic acid from opium

13. 5g. of opium are triturated with 2 ml acetone which facilitates the breaking down of sticky lumps and, drying off during the process, leaves the opium as a friable powder readily accessible to the action of extracting solvents.

14. The powdered material is well stirred with 30 ml acetone and allowed to stand for an hour. The mixture is then filtered with suction, and the residue percolated with a further 20 ml acetone. The combined acetone portions are evaporated to dryness, and extracted by thorough stirring with dilute hydrochloric acid (20 ml of N/2 is a convenient amount) and subsequent washing with water. To the filtered extract, N.NaOH is gradually added until a permanent precipitate just forms. A few gm. of sodium acetate are then stirred in and the mixture allowed to stand until the supernatant liquid is clear. The solid is filtered off under pressure, washed with dilute NaOH and with water, sucked as dry as possible and finally washed through with acetone into a dry receptacle in which it is evaporated and weighed after drying at 100°.

15. The opium residue from the acetone extraction is shaken with successive portions of 30-40 ml of water at about 60° until the aqueous extract shows not more than faint turbidity with barium chloride solution (normally three portions suffice).

II. Precipitation of narcotine and of trisodium meconate

16. Sodium acetate is stirred into the filtered aqueous extract until it is alkaline to methyl red. After standing until the supernatant liquid is clear, the solid is filtered off and washed with a little water. To the filtrate, 1-2g barium chloride dissolved in a little hot water is added. The solid is washed with about 25 ml acetone and the residue reserved for treatment along with the barium meconate precipitate. The acetone washings are diluted largely with water, and the precipitated narcotine filtered off, washed with dilute NaOH and evaporated and dried as before. The weight of narcotine so obtained, added to that obtained under I. above, represents the total narcotine in the opium.

17. The precipitate formed by adding barium chloride to the filtered aqueous extract is filtered off and washed with a little water, and the small insoluble residue from the narcotine precipitation added to it as noted above. It is then broken up with 10 ml N. Sulphuric acid. After standing for an hour, 1g of

/sodium

sodium bicarbonate is stirred in, and the liquid filtered off. The residue is washed with two portions each of 7-8 ml water.

18. To the filtrate and washings, 2 ml N. sodium hydroxide are added, and solid sodium chloride is gradually stirred in until a little remains undissolved. After standing for a few hours, the precipitated trisodium meconate is filtered off and washed with 50 per cent aqueous alcohol, saturated with sodium chloride, until the washings are colourless and neutral to phenolphthalein. The residue should be a granular powder of a clear lemon-yellow and when dissolved in 20 ml N/10 sulphuric acid should show little or no brown or red colour; it may then be back-titrated to brom-phenol blue with N/10 sodium hydroxide; 1 ml N/10 acid is equivalent to 0.020g meconic acid. If the solution before titration is noticeably discoloured, reprecipitation by making alkaline and again salting out is an effective means of purification and involves no significant loss.